Ventricular Catheter Systems with Subcutaneous Reservoirs (Ommaya Reservoirs) in Pediatric Patients with Brain Tumors: Infections and Other Complications

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Abstract: Objective This study aims to describe complications related to ventricular catheter systems with subcutaneous reservoirs (VCSR) (such as Ommaya reservoirs) in pediatric patients with brain tumors. Methods Retrospective analysis of consecutive patients with a total of 31 VCSR treated at the Children's University Hospital of Zurich, Switzerland. Results A total of 20 patients with a median age of 3.3 years at VCSR implantation received 31 VCSR. Overall, 19 complications in 11 patients were recorded: 7 patients had a VCSR-related infection with coagulase-negative staphylococci, 4 of these probably as a surgical complication and 3 probably related to VCSR use. Systemic perioperative prophylaxis was administered in 22 cases, and intraventricular vancomycin and gentamicin were given in 8 cases (none of which subsequently developed an infection). Other complications included wound dehiscence, catheter malplacement, and leakage of cerebrospinal fluid. Overall, 17 VCSR were explanted due to complications. Conclusion Infections were the most frequent VCSR-related complication. In our own institution, the high rate of complications led to the definition of a bundle of measures as a standard operating procedure for VCSR placement and use. Prospective studies in larger patient collectives are warranted to better identify risk factors and evaluate preventive measures such as the administration of perioperative antibiotics and the use of antimicrobial coating of catheters.

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Ventricular Catheter Systems with Subcutaneous Reservoirs in Pediatric Patients with Brain Tumors: Infections and Other Complications

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ABSTRACT

OBJECTIVE: To describe complications related to ventricular catheter systems with subcutaneous reservoirs (VCSR) (such as Ommaya reservoirs) in pediatric patients with brain tumors.
METHODS: Retrospective analysis of consecutive patients with a total of 31 VCSR treated at the Children's University Hospital of Zurich.
RESULTS: Twenty patients with a median age of 3.3 years at VCSR implantation received 31 VCSR. Nineteen complications in 11 patients were recorded: Seven patients had a VCSR-related infection with coagulase-negative staphylococci, 4 of these probably as a surgical complication and 3 probably related to VCSR use. Systemic perioperative prophylaxis was administered in 22 cases, and intraventricular vancomycin and gentamicin were given in 8 cases (none of which subsequently developed an infection). Other complications included wound dehiscence, catheter malplacement, and leakage of cerebrospinal fluid. Seventeen VCSR were explanted due to complications.
CONCLUSION: Infections were the most frequent VCSR-related complication. In our own institution, the high rate of complications led to the definition of a bundle of measures as a SOP for VCSR placement and use. Prospective studies in larger patient collectives are warranted to better identify risk factors and evaluate preventive measures such as the administration of perioperative antibiotics and the use of antimicrobial coating of catheters.

INTRODUCTION

Malignant brain tumors in childhood, such as medulloblastoma, ependymoma, or atypical teratoid/rhabdoid tumors, have the propensity to disseminate within the cerebrospinal fluid (CSF) space. Overt metastatic disease may be present already at diagnosis or at relapse. After surgery, adjuvant treatment of such tumors often includes radiotherapy and systemic chemotherapy. However, radiotherapy, especially craniospinal irradiation in young children, can lead to significant long-term sequelae, such as neuropsychological impairment or secondary malignancies, and penetration of chemotherapy into the CSF space is limited by the blood-brain barrier.(1-3) Therefore, several childhood brain tumor treatment protocols include intraventricular chemotherapy with drugs such as methotrexate, cytarabine, etoposide, and topotecan administered into the CSF space through a ventricular catheter system with a subcutaneous reservoir (VCSR) allowing to defer or obviate radiotherapy in some patients or to complement multimodal therapy in others.(4-8)

The instillation of chemotherapy into a lateral ventricle using a VCSR such as the Ommaya reservoir offers several potential advantages compared to lumbar intrathecal injection.(9) It ensures a more uniform drug distribution within the CSF, requires a lower minimum thrombocyte count, and is more convenient for the patients, who generally do not need sedation or anesthesia. (10-11) However, the implantation and the use of VCSR may be associated with complications such as misplacement, intracerebral hemorrhage, and infection. Several series, most of them describing adult patients, found a large variability in complication rates, ranging from almost 0% to more than 40%.(12-22) The reasons for this strikingly wide range as well as the potential role preventive measures (e.g. perioperative antimicrobial prophylaxis or antimicrobial catheter impregnation) are still poorly understood. To study the incidence and nature of complications related to VCSR in patients with pediatric brain tumors, we conducted a retrospective analysis of 20 consecutive patients treated in our institution in whom a VCSR was implanted between 1996 and 2011.

METHODS

A retrospective study was undertaken on 591 consecutive children up to the age of 16 years with a primary brain tumor admitted to the University Children's Hospital of Zurich, Switzerland, from January 1980 to December 2011. Twenty-one of these patients received a VCSR, all of them between 1996 and 2011. One of these patients declined to participate in clinical trials; therefore, clinical information of 20 patients was extracted from the patient files and analyzed.

Intraventricular chemotherapy and intraventricular saline were filled into sterile syringes in a laminar flow hood by trained nurses. Application of chemotherapy to the VCSR was performed by 6 trained pediatric oncology consultants (in the majority of cases by 2 neuro-oncology consultants) as follows: All persons in the treatment room apart from the patient wore a mask and the physician performing the injection used sterile gloves; scalp hair growing above the reservoir was slightly shortened but not shaved; for disinfection a solution containing either propanol (mostly used in earlier patients) or a solution containing propanol + octenidine dihydrochloride (in later patients) was applied for six times, each time spirally wiping a soaked sterile cotton swab. The reservoir was punctured with a 22 Gauge Huber needle connected to an empty syringe with a short connection tube, approximately 2 to 3 ml of CSF were aspirated and discarded, the chemotherapy agent (in most patients methotrexate) was administered, the system was flushed with approximately 2 ml aqueous sodium chloride solution (0.9%), and after removal of the needle the puncture site was covered with a sterile dry patch. VCSR-related infection was defined as presence of both clinical signs of infection (i.e. fever, headache, meningism, nausea, vomiting, or signs of local tissue infection overlying the reservoir) and positive cultures of CSF (obtained through the VCSR or, if not analyzed, by lumbar puncture) or positive cultures on microbiologic examination of the VCSR after explantation. Date of infection was defined as the date of the appearance of the first clinical sign, and date of complication other than infection as the date of detection of the complication.

Kaplan-Meier estimates were used for the probability of VCSR survival (PVS) free of complication-related explantation with time for PVS measured from implantation to explantation or last follow-up, whichever came first, and indicated as percentage followed by the standard error. PVS were compared using the log-rank test. Fisher's exact test was used to analyze the correlation between complication status and dichotomous variables (e.g. use of perioperative systemic antimicrobial prophylaxis, intrathecal antimicrobial prophylaxis, and antimicrobial catheter impregnation). Mann-Whitney-U test was used to examine the correlation between complication status and continuous variables (e.g. neutrophil count at implantation). All p-values were considered as exploratory, no significance level was fixed. Analyses were performed with IBM SPSS Statistics software, version 20.

RESULTS

Patient characteristics, implantation procedure, VCSR use and VCSR status at last follow-up

Twenty pediatric patients with malignant brain tumors received a total of 31 VCSR between April 2000 and May 2011 (median number of VCSR per patient, 1; range, 1 to 3). Patient and VCSR implantation and use characteristics are summarized in Table 1 and Table 2. The median age at VCSR implantation was 3.3 years (range, 1.4 to 11.7), and the median time between last tumor surgery and VCSR implantation was 22 days (range, 0 to 217). The reservoirs were implanted by 11 different neurosurgeons. While perioperative systemic antimicrobial prophylaxis was documented in the majority of procedures (22/31; cefazolin [25 mg/kg] in 21, and ceftriaxone [25 mg/kg] in 1 case, each patient receiving a single dose between 60 and 30 minutes before first skin incision), intraoperative intraventricular antimicrobial prophylaxis with gentamicin (3 mg/dose) and vancomycin (3 mg/dose) was given in 8/31 cases only. In 3 patients, a catheter with antimicrobial impregnation (rifampicin and clindamycin [Bactiseal®, Johnson & Johnson, Raynham, MA]) was implanted. Absolute neutrophil blood count at implantation was 4.4 G/L (median; range, 0.9 to 26.7). None of the patients received perioperative corticosteroids. Median time from VCSR implantation to first use was 2.5 days (range, 0 to 34). The total number of VCSR survival days was 16'868 (median per device, 155 days; range, 2 to 2'871), the total number of chemotherapy injections 461 (median number per VCSR, 9; range, 0 to 37). All patients also received systemic chemotherapy, 7/20 patients received radiotherapy at some point during the treatment course. VCSR status at last follow-up: 17, explanted due to complication; 2, explanted due to non-use; 4, in situ, patient alive; 8, not explanted, patient dead of disease.

Complications

Nineteen complications occurred in 18/31 VCSR (58%) in 11/20 patients (55%), leading to the removal of 17 VCSR after a median of 55 days (range, 2 to 584) (Table 3). Seven infections (23% of VCSR) with coagulase-negative staphylococci were diagnosed at a median of 10 (range, 2 to 203) days after implantation in 7 different patients, with positive CSF cultures in all patients (in one patient, only lumbar CSF was examined), positive cultures at microbiologic examination of the explanted VCSR (6/7), pleocytosis in 5/5 patients (no data available in 2 patients), and clinical symptoms of infection in all patients. Four infections were diagnosed within 10 days after surgery (after 0 to 2 intraventricular chemotherapy injections), therefore most probably related to surgery/perioperative measures, while 3 infections were diagnosed between 51 to 203 days after implantation (after 9 to 29 injections) and therefore suspected to be caused by VCSR use. Median time from VCSR implantation to first use was 3.5 days [range, 2 to 5 days] in those 4 patients who received at least 1 chemotherapy injection. According to institutional policy, all the VCSR with infection were explanted, and patients were treated with systemic antibiotics (mostly vancomycin and/or ceftriaxone) in 6/7 cases and with intraventricular vancomycin in 5/7 cases. All infections resolved without sequelae. No correlation between systemic perioperative antimicrobial prophylaxis and the risk of infection was observed, however, there was a trend towards a smaller risk in patients who received intraventricular antimicrobial prophylaxis with none

of the 8 patients with prophylaxis developing an infection, whereas 7/23 without intraventricular prophylaxis eventually did (p=0.146). No influence of age or of neutrophil count at implantation was found, however, none of the patients was neutropenic at the time of surgery (lower range of neutrophil count, 0.9 G/L). No correlations could be shown between the line of therapy (first-line vs. second-line), the stage of the disease (non-metastatic vs. metastatic) at the time of implantation, or the time from VCSR implantation to its first use on one hand with the development of complications or specifically with infections on the other hand. The number of injections was not correlated with the development of infection more than 10 days after placement (3 patients), however, these figures can only be interpreted with caution as the development of infection with subsequent explantation reciprocally influences the total number of injections. One patient with a positive CSF culture (coagulase-negative staphylococcus), however without pleocytosis or clinical signs of infection was not treated nor was the VCSR removed. Subsequent CSF cultures remained negative, and the episode was interpreted as contamination instead of infection.

Non-infectious complications included wound dehiscence in 6 (19%), catheter malplacement in 3 (10%), and CSF leakage and subcutaneous CSF collection in 1 (3%) case each, leading to explantation in all but the last patient. In another patient, who needed a ventriculoperitoneal (VP) shunt for a communicating hydrocephalus after tumor surgery as an emergency procedure, the VCSR, which had been placed two days before, was removed in the same procedure. Even though, in retrospect, removal might not have been necessary, it has been counted as a complication in this analysis.

The 1 year-probability of VCSR survival (PVS) without complication-related explantation was 48% (±9%) (Table 4 and Figure 1A), and the 1 year-PVS without infection-related explantation was 73% (±9%) (Figure 1B). When potential risk factors for infection were explored in univariable analyses using the log-rank test, administration of perioperative intraventricular antimicrobial prophylaxis emerged as the strongest protective factor (1 year-PVS free of infection of 100% vs. 66%[±11%], p=0.123) (Figure 1C).

DISCUSSION

Ventricular catheters with subcutaneous reservoirs (VCSR), such as the Ommaya reservoir, are used in children with brain tumors to deliver chemotherapy directly to the CSF space thereby overcoming the blood-brain barrier. Publications on VCSR-related complications, such as malplacement, hemorrhage, and infections related to surgery and to use, have described a large variability in complications rates in adult patients with cancer.(12-14, 16-18, 20, 22-23) However, literature on VCSR-related complications in children with brain tumors is scarce.(15, 19) We present a retrospective analysis of 20 consecutive patients with a total of 31 VCSR diagnosed at our institution between 1996 and 2011, describing the incidence and nature of VCSR-related complications and trying to identify predisposing factors.

We found a complication rate of 58% leading to the removal of 55% VCSR. While infections were the most common complications, others included wound dehiscence, malplacement, and cerebrospinal fluid leakage. The probability of 1-year VCSR survival (PVS) free of explantation due to complication was 48%. Our complication rate is higher than that of most other publications, including the two pediatric series: In 143 patients receiving intraventricular radioimmunotherapy Kramer et al. found 5 (3%) complications, mostly malfunction by a 'migrating catheter tip' and catheter-associated cyst formation, which eventually lead to the removal of the device. None of the patients had a VCSR-related infection.(15) Peyrl et al. described a series of 98 pediatric patients with brain tumors and VCSR receiving chemotherapy. They found a complication rate of only 5% (malplacement, malposition of the catheter tip after shrinkage of the ventricles, dysfunction due to kinking of the catheter, disconnection of the catheter, and infection).(19)

In accordance with most of the other series, the most frequent complications were infections (23% of VCSR), with four early infections (2 to 10 days after implantation) most probably as a complication of surgery and three later occurring infections (51 to 203 days after implantation), probably due to the use of the device. The 1-year PVS free of infection was 73%. The causative agents were coagulase-negative staphylococci in all cases, and according to our institutional policy, all VCSR were explanted and the patients were treated with systemic and/or intraventricular antibiotics. While the frequency of infectious complications shows a marked variation in other publications ranging from 0% to 30% in most cases, the uniformly most frequent causative agents are coagulase-negative staphylococci. More rarely, species such as P. acnes, S. aureus, E. faecalis, and P. aeruginosa have been described.(12-14, 17, 23-24) Comparability is somewhat limited not only by patient heterogeneity, but also by the lack of uniformly accepted definition of VCSR-related infection.

For ventriculo-peritoneal shunts, the usefulness of perioperative systemic antimicrobial prophylaxis has been shown, even if the optimum regimen is not known yet.(25-27) Impregnation of catheters with antibiotics may have a beneficial effect as well,(28) but there is no data allowing any conclusions on the efficacy of intraventricular antimicrobial prophylaxis. To our knowledge, no conclusive data on the usefulness of antimicrobial prophylaxis for VCSR has been published. In our sample, no correlation between systemic perioperative antimicrobial prophylaxis or antimicrobial impregnation of catheters and

infection could be shown. However, a trend towards a correlation between perioperative intraventricular antimicrobial prophylaxis with gentamicin and vancomycin emerged: While seven of 23 patients (30%) without prophylaxis eventually developed an infection, none of those eight patients with intraventricular prophylaxis did (p=0.146). While in view of the small sample size and the retrospective design these results do not allow to draw definitive conclusions, the difference between the groups with or without intraventricular prophylaxis seems to support the hypothesis that systemic antimicrobial prophylaxis might not be sufficient in the implantation of foreign material into the CSF space. While it may reduce the risk for wound contamination by direct inoculation and/or by bacteremia, systemic antibiotic prophylaxis may possibly not reach a sufficiently high concentration within the CSF to prevent contamination of the catheter. This might be overcome by adding an intraventricular prophylaxis, e.g. with a combination of vancomycin and gentamicin, which offers a broad coverage of potential pathogens including coagulase-negative staphylococci.

To our knowledge, no thorough analyses of the influence of other protective measures or risk factors have been conducted. We could not detect any influence of other parameters such as age, neutrophil count at implantation, or number of injections into the reservoir, on the risk of infection, however due to the small sample size the power of these calculations is only very limited. While we found infections in 23% of VCSR, only one infection was reported in the series of Peyrl et al., which is the only publication on a patient collective comparable similar to ours.(19) A few institutional differences regarding implantation and use can be found: While in our institution systemic perioperative antimicrobial prophylaxis generally consists of a single dose of cefazolin as a perioperative prophylaxis, their patients received antibiotics for three to five days after surgery. We had not set any minimum interval between the VCSR implantation and its first use, whereas the first injection was not done earlier than 5 days postoperatively in their patients. Moreover, we used 22 Gauge Huber needle for injections as opposed to a thinner (25 Gauge) butterfly cannula, and whereas we didn’t shave the scalp over the reservoir they did. Whether one or more of these differences has contributed to the higher frequency of infections in our patients, cannot be determined from available data.

Controversies exist regarding the optimum management of VCSR infections. While in all of our patients with overt VCSR infection the device was explanted at diagnosis of the complication, others have tried to rescue the VCSR using intravenous ± intraventricular antimicrobials with various rates of success.(13, 16-17, 24, 29) Whether a VCSR that is used anymore should be left in place or electively explanted is another still unanswered question. Whereas the existence of late infections occurring several years after the last use of the device(23, 30-31) would serve as an argument in favor of explantation, the (non-quantified) risk of hemorrhage at explantation due to the adhesion of CNS/choroid plexus tissue to the catheter can be cited as a counterargument (even if ideally the implanted catheter tip does not reach the choroid plexus).

Non-infectious complications leading to VCSR explantation in our series included wound dehiscence, catheter malplacement, and CSF leakage. A subcutaneous CSF collection after VCSR implantation resolved spontaneously, and in one patient the VCSR was removed during ventriculo-peritoneal shunt

implantation performed as an emergency procedure due to malresorptive hydrocephalus after tumor surgery. Wound dehiscence was not a frequent complication in other series. Possible preventive measures to avoid high traction on the suture may be the choice of small reservoir sizes in young children, the preparation of a sufficiently large subcutaneous pocket at implantation, and the avoidance of placement of the reservoir or the extracranial end of the catheter directly under the site of incision. Catheter malplacement has been described as one of the more frequent complications by several other authors.(13, 16, 18-20) In one of our patients, the catheter had not been advanced far enough, so that the tip was located in the brain parenchyma. Nevertheless, aspiration of CSF was possible due to a communication with the external CSF space. In order to prevent instillation of chemotherapy into a misplaced system, we therefore recommend a verification of a correct catheter position by imaging before the first drug injection. Catheter malplacement could possibly be avoided by techniques such as navigation-guided placement. However, it is not known whether a consequent extension of the duration of the surgical procedure would have adverse effects such as a higher risk of surgical infections.(32-33)

To our knowledge, this series is one of the three only publications of VCSR-related complications in a collective of children with brain tumors, therefore only limited comparison of our figures to those of others are possible. Nevertheless we conclude that we found an unacceptably high rate of complications, consisting predominantly of device-related infections, but also of wound dehiscence, malplacement and others. Due to the restricted patient and reservoir number and due to the retrospective nature of our analysis it is not possible to identify one or a few main risk factors for each of these complications. After analysis of this series we therefore defined a bundle of measures as a SOP for preoperative, intraoperative, and postoperative management of VCSR placement and use, with the idea that this SOP may contribute to a risk reduction and at the same time allow a prospective analysis of uniformly handled VCSR. Among others, these measures include: implantation only in patients with neutrophil count of at least 0.5 G/l at [and expectedly until at least 5 days after] implantation; if possible no perioperative steroids or other immunosuppressants; surgery only by the most experienced pediatric neurosurgeon (in case of absence the smallest number of other surgeons possible); perioperative antimicrobial prophylaxis with intravenous cefazolin plus intraventricular gentamicin and vancomycin; choice of impregnated catheters encouraged; extra small reservoir size for young children and generous mobilization of skin at implantation to avoid skin traction; first puncture not earlier than 5 days after implantation; punctures if possible always by the same two neuro-oncologists, in any case only by trained senior oncology consultants; hair above reservoir carefully cut with scissors; masks for each person except for patient; closed door and windows during whole procedure; disinfection with a solution containing octenidine dihydrochloride and propanol as follows: six times spirally rubbing a soaked sterile cotton swab, thereafter applying a soaked sterile compress during 2 minutes before letting the skin dry completely; use of a non-coring 25 G needle connected to a sterile syringe with a short connection tube; aspiration of 2 ml of CSF, injection of chemotherapy, flushing with 2 ml saline using an industrially pre-filled syringe.

Prospective studies to identify risk factors for complications and protective measures are warranted, notably regarding the optimum administration of perioperative intravenous and intraventricular

antibiotics as well as the use of antimicrobial impregnation of catheters, which could be assessed in a randomized manner.

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LEGENDS TABLES AND FIGURE

TABLE 1. Characteristics of 20 patients with a total of 31 ventricular catheters with subcutaneous reservoirs (VCSR)

TABLE 2. Characteristics of VCSR implantation and use

TABLE 3. Characteristics of complications in 20 patients with a total of 31 VCSR

TABLE 4. Probabilities of 1-year VCSR survival free of complication-induced explantation (1-year VSFCIE) in 20 patients with a total of 31 VCSR

FIGURE 1. A Probability of VCSR survival free of explantation due to complication (31 VCSR in 20 patients). B Probability of infection-free VCSR survival (31 VCSR in 20 patients). C Probability of infection-free reservoir survival depending on the application of perioperative intraventricular antibiotic prophylaxis (31 VCSR in 20 patients)

TABLE 1. Characteristics of 20 patients with a total of 31 ventricular catheters with subcutaneous reservoirs (VCSR)

Number of patients	
	20
Sex	
	12 (60%) Male
	8 (40%) Female
Age at diagnosis	
(years; median, range)	2.7 (1.4 -11.6)
Tumor histology	
	12 (60%) Medulloblastoma
	3 (15%) Central nervous system primitive neuroectodermal tumor
	3 (15%) Atypical teratoid/rhabdoid tumor
	1 (5%) Glioblastoma multiforme
	1 (5%) Malignant melanocytic tumor
Metastatic disease at VCSR implantation	
	16 (80%) No
	4 (20%) Yes
Line of therapy at VCSR implantation	
	16 (80%) first-line
	4 (20%) second-line (i.e. at progression/relapse)
Survival status of patient at last follow-up	
	7 (35%) Alive
	13 (65%) Dead of disease
Number of VCSR per patient	
(median, range)	1 (1-3)

TABLE 2. Characteristics of VCSR implantation and use

	VCSR without infection	VCSR with infection	p-value
	n=24	n=7	
Age at VCSR implantation (years; median, range)	3.8 (1.4-11.7)	2.6 (1.5-9.5)	0.473
Perioperative intraventricular antimicrobial prophylaxis (gentamicin + vancomycin)			
	16 (67%) No	7 (100%) No	0.146
	8 (33%) Yes	0 (0%) Yes	
Perioperative intravenous antimicrobial prophylaxis (cefazolin, n=21; ceftriaxone, n=1)			
	7 (29%) No	2 (29%) No	1.000
	17 (71%) Yes	5 (71%) Yes	
Perioperative antimicrobial prophylaxis (intraventricular and/or intravenous)			
	5 (21%) No	2 (29%) No	0.642
	19 (79%) Yes	5 (71%) Yes	
Antimicrobial impregnation of catheter (rifampicin + clindamycin)			
	12 (50%) No	2 (29%) No	0.572
	2 (8%) Yes	1 (14%) Yes	
	10 (42%) Unknown	4 (57%) Unknown	
Antimicrobial impregnation and/or perioperative antimicrobial prophylaxis			
	3 (13%) No	1 (14%) No	0.795
	19 (79%) Yes	5 (71%) Yes	
	2 (8%) Unknown	1 (14%) Unknown	
Absolute neutrophil blood count at implantation (G/L; median, range)	3.25 (0.9 - 26.7)	5.1 (2.4 - 8.3)	0.258
Number of chemotherapy injections per VCSR (Only VCSR without early [≤10 days after explantation] infection) (median, range)	20 (0 - 37)	10 (9 - 29) *(n=3)*	0.786

TABLE 3. Characteristics of complications in 20 patients with a total of 31 VCSR

Number of VCSR with complications	18 in 11 (58% of implanted VCSR, 55% of patients)
Number of complications	19
	7 Infection with coagulase-negative staphylococci
	6 Wound dehiscence
	3 Malplacement
	1 Subcutaneous CSF collection
	1 Cerebrospinal fluid leakage
	1 Hydrocephalus*
Number of complications leading to VCSR explantation	17 in 11 patients (55% of implanted VCSR, 55% of patients)
Interval between implantation and diagnosis of complication leading to explantation	
(days; median, range)	
All VCSR (n=18)	51 (2 - 584)
VCSR with infection (n=7)	10 (2 - 203)
VCSR with other complication (n=10)	61 (2 - 584)
Interval between implantation and complication-related explantation	
(days; median, range)	
All VCSR (n=18)	55 (2 - 584)
VCSR with infection (n=7)	11 (2 - 226)
VCSR with other complication (n=10)	61 (2 - 584)
Infections (n=7)	
Causative agent	7 Coagulase-negative staphylococci
Time point of diagnosis of infection (days after implantation)	
(days; median, range)	
All VCSR	10 (2 - 203)
Early (post-operative) infections (n=4)	3 (2 - 10)
Later occurring infections (n=3)	66 (51 - 203)
Interval between diagnosis of infection and explantation	
(days; median, range)	1 (0 - 23)
Antimicrobial treatment duration of infection	
(days; median, range)	10 (3 - 30)
Antimicrobial regimen	
2 Ceftriaxone + intraventricular vancomycin	
2 Ceftriaxone + vancomycin	
1 Rifampicin + vancomycin + intraventricular vancomycin	
1 Teicoplanin + intraventricular vancomycin	
1 Intraventricular vancomycin	

* Hydrocephalus due to tumor surgery, however counted as a complication as surgeon decided to remove the VCSR when ventriculo-peritoneal shunt was inserted

TABLE 4. Probability of 1-year VCSR survival free of complication-induced explantation in 20 patients with a total of 31 VCSR

	Only infections		All complications	
	% (standard error)	p-value	% (standard error)	p-value
All VCSR (n=31)	73 (9)		48 (9)	
Age at implantation				
Above median (n=15)	83 (12)	0.329	40 (13)	0.323
Below/at median (n=16)	65 (13)		55(13)	
Perioperative intraventricular antimicrobial prophylaxis (gentamicin + vancomycin)				
No (n=23)	66 (11)	0.123		
Yes (n=8)	100			
Perioperative intravenous antimicrobial prophylaxis (cefazolin, n=21; ceftriaxone, n=1)				
No (n=9)	78 (14)	0.753		
Yes (n=22)	70 (12)			
Perioperative antimicrobial prophylaxis (intraventricular and/or intravenous)				
No (n=7)	71 (17)	0.849		
Yes (n=24)	74 (11)			
Antimicrobial impregnation of catheter (Bactiseal: rifampicin + clindamycin)				
No (n=14)	83 (12)	0.500		
Yes (n=3)	67 (27)			
Unknown (n=14)	68 (14)			
Antimicrobial impregnation and/or perioperative antimicrobial prophylaxis				
No (n=4)	75 (22)	0.934		
Yes (n=24)	74 (11)			
Unknown (n=3)	67 (27)			
Absolute neutrophil blood count at implantation				
Above median (n=15)	62 (14)	0.225		
Below/at median (n=16)	86 (9)			
Number of chemotherapy injections per VCSR (VCSR with early infection [≤10 days after implantation, therefore probably surgical complication excluded])				
Above median (n=13)	91 (9)	0.199		
Below/at median (n=14)	76 (15)			

FIGURE 1A: Probability of VCSR survival free of explantation due to complication (31 VCSR in 20 patients)

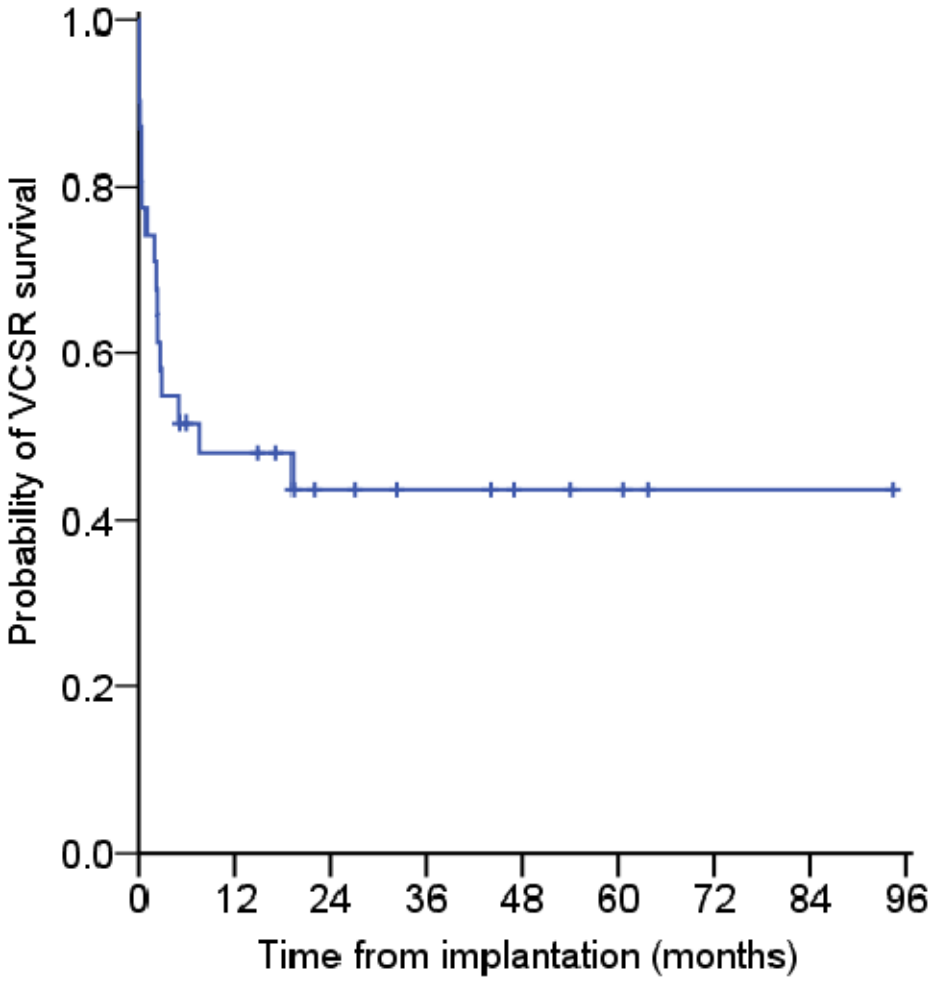

FIGURE 1B: Probability of infection-free VCSR survival (31 VCSR in 20 patients)

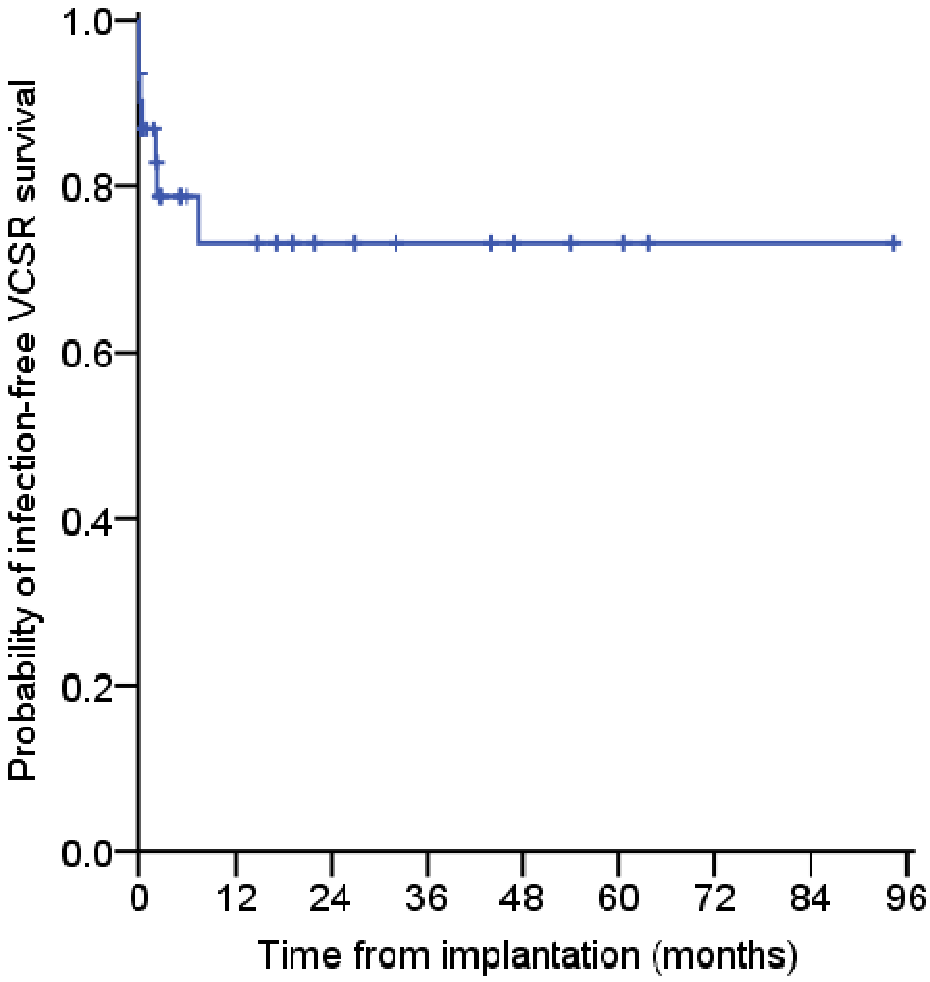

FIGURE 1C: Probability of infection-free VCSR survival depending on the application of perioperative intraventricular antimicrobial prophylaxis (31 VCSR in 20 patients)